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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,621	02/15/2006	Judy Lieberman	033393-055184	1751

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EXAMINER	
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ART UNIT	PAPER NUMBER
1635	

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11/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,621	LIEBERMAN ET AL.	
	Examiner	Art Unit	
	Jennifer Pitrak	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2007*.

a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62-76* is/are pending in the application.

4a) Of the above claim(s) *68 and 71-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62-67, 69, and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

0)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

1)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

2)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/29/05; 09/26/05; 07/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 62-70, drawn to a method for treating or preventing a viral infection by administering siRNAs against CCR5 in the reply filed on 09/20/07 is acknowledged.

In response to the species election, Applicants elected HIV as a virus and liposomes as a pharmaceutical carrier.

In response to the sequence restriction, Applicants elected SEQ ID NO: 1 (sense) and SEQ ID NO: 2 (antisense) of an siRNA directed to human CCR5.

Claims status

Claims 71-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 09/20/07.

Claim 68 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 09/20/07.

Claims 62-67 and 69-70 are currently being examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 62-67 and 69-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a viral infection with a formulation comprising CCR5-directed siRNAs, does not reasonably provide enablement for preventing a viral infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are to a method of treating or preventing HIV infection as described above.

The specification describes the use of CCR5 siRNAs comprising SEQ ID NOs: 1 and 2 in cultured MDM cells, wherein the siRNAs were transfected into the cells (p.41) and reduced subsequent HIV infection of the cells. The specification provides no evidence for the use of siRNAs to prevent HIV infection in an individual. Currently, the state of the art indicates that HIV prevention has yet to be achieved. For example, a recent review article summarizes the state of HIV prevention as follows: "Ultimate control of the HIV epidemic will require prevention of new infections, and as the global epidemic continues to expand, there has never been a greater need for an effective vaccine. Developing an effective AIDS vaccine that prevents infection may not be feasible, so current vaccine strategies are focused on protection from disease progression," (Deeks, S.G. and B.D. Walker, Immunity, v.27:406-16, 2007). Thus, Applicant's claims to prevention of HIV are not enabled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 62, 63, 67, 69, and 70 are rejected under 35 U.S.C. 102(e) as being anticipated by Beresford, *et al.* (US 2004/0248296).

The applied reference has a common assignee and inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claims are to a method for treating or preventing HIV infection comprising administering to an individual a formulation comprising siRNAs against the host cell receptor, CCR5, wherein the formulation comprises liposomes and is either a topical or intravaginal formulation.

Application Beresford, *et al.* claim a method of treating or preventing HIV infection comprising administering an siRNA targeting a host cell receptor transcript (claims 87 and 88). Beresford, *et al.* further disclose that the inventive compositions may be formulated for

transdermal (topical) and vaginal (paragraph [0097]) delivery, and describe liposomes as pharmaceutically acceptable carriers for the siRNA compositions (paragraph [0106]).

Thus, the reference anticipates the instant claims 62, 63, 67, 69, and 70.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 62, 63, 65, 67, 69, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takaku, *et al.* (1999, JP11-292795) and Novina, *et al.* (2002, Nat. Med. v.8:681-686).

The claims are drawn to a method for treating or preventing HIV infection in an individual who has or who is at risk of having HIV comprising administering a formulation comprising siRNAs directed against the CCR5 gene (claims 62 and 63), liposomes (claim 67), and further comprising siRNAs directed against the HIV p24 gene (claim 65), wherein the administration is topical or intravaginal (claims 69 and 70).

Takaku, *et al.* teach antisense oligonucleotides directed against CCR5 and for use as prophylaxis against HIV infection. Takaku, *et al.* claim HIV cofactor inhibitors that contain oligonucleotides complementary to the CCR5 gene and that the claimed inhibitors can be used for prophylaxis against HIV infection and/or for HIV infection therapy (Claim 1 and beginning of "Detailed Description of the Invention"). Specifically, Takaku, *et al.* teach the antisense

oligonucleotide comprising SEQ ID NO: 47 (Figure 1), which, as shown below, is complementary to the mouse CCR5 gene sequence from position 855 to position 874.

```
M. musculus CCR5    (855)5'-ACCTTCCAGGAATTCTTTGG-3'(874)
                             ||||||||||||||||||||
SEQ ID NO: 47              3'-TGGAAGGTCCTTAAGAAACC-5'
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Takaku, *et al.* further teach that such therapeutic oligonucleotides can be formulated with liposomes and can be administered orally, parenterally, or locally and in the form of lotions, ointments, and suppositories (paragraph [0029]). Takaku, *et al.* do not teach the use of siRNAs to treat or prevent HIV infection, nor do they specifically teach topical or intravaginal administration.

Novina, *et al.* teach the use of siRNAs for prevention and therapy against HIV infection. Novina, *et al.* teach siRNAs directed to the mRNA encoding the HIV receptor, CD4, inhibits viral entry into host cells (p.681, Figure 1, and Figure 6) and that CCR5 "may be the preferred coreceptor target" for siRNA targeting (p.684, first paragraph of Discussion). Novina, *et al.* also teach siRNAs directed against the HIV p24 gene decreased HIV infection of HeLa cells (p.681-2 and Figure 2). Novina, *et al.* further suggest siRNA technology as a possible therapeutic strategy to inhibit HIV replication in host cells and that strategies that target combinations of viral genes and cellular genes may provide improvements to RNA-based antiviral therapies (p.685).

It would have been obvious to one of ordinary skill in the art at the time of the instant application to target the CCR5 gene, as taught by Takaku, *et al.*, with siRNAs, as taught by Novina, *et al.*, for the treatment of HIV infection. It further would have been obvious to target the p24 gene in combination with CCR5, given the motivation from Novina, *et al.* to combine

siRNAs targeting viral and cellular genes. It would have been obvious to treat HIV infection by topically or intravaginally administering liposomal formulations of CCR5-targeting siRNAs because Takara *et al.* teach local delivery of the antisense formulations, which include lotions and ointments, which are topical formulations, and formulations that also include suppositories, which are intravaginal formulations. Based on Takara, *et al.*'s teaching of antisense-targeting of CCR5, one would have had a reasonable expectation that siRNA-targeting of CCR5 would effectively treat HIV infection. Thus, the claims as a whole would have been obvious to one skilled in the art at the time of the instant application.

Allowable Subject Matter

SEQ ID NOs: 1 and 2 are free of the prior art.

Closing

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Pitrak whose telephone number is 571-270-3061. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak
Patent Examiner
Art Unit 1635

Tracy Vivlemore
Examiner, AU 1635